NUCLEIC ACID CHEMISTRY

IMPROVED AND NEW SYNTHETIC PROCEDURES, METHODS AND TECHNIQUES

PART TWO

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[103] 8,2'-ANHYDRIDES OF PURINE-8-THIOL NUCLEOSIDES (OR OF PURINE 2'-THIONUCLEOSIDES)

Synthesis of 8,2'-Anhydronucleosides of Purine-8-thiol [or of 8,2'-Anhydro-(2'-thionucleosides)] by Use of Diphenyl Carbonate as the Cyclizing Agent

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INTRODUCTION

Purine anhydronucleosides that have an anhydride ring between C-8 of the purine residue and a hydroxyl group of the glycosyl group are useful intermediates for the modification of the sugar moieties.[1] Especially, 8,2'-anhydronucleosides of purines are important compounds for the synthesis of 2-deoxy-D-*erythro*-pentosylpurines. The method described here is convenient for the large-scale preparation of 8,2'-anhydrides of purine-8-thiol nucleosides [8,2'-anhydro-(2'-thionucleosides)] by use of diphenyl carbonate as the cyclizing agent.[a]

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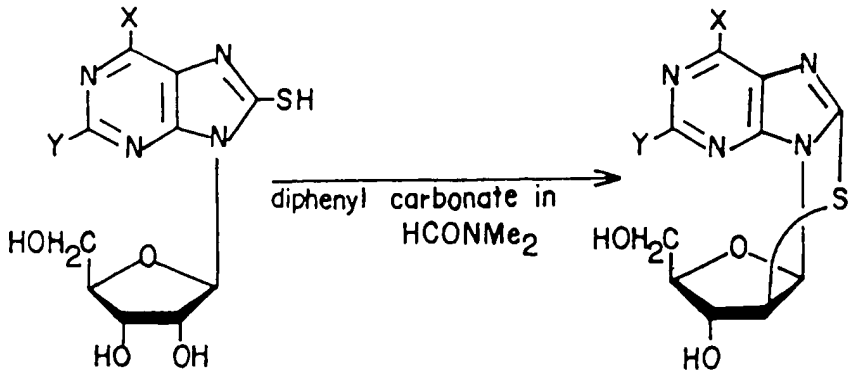
[a] Ikehara and coworkers[2] reported that the method using diphenyl carbonate as the cyclizing agent is also applicable to the synthesis of 8,2'-anhydronucleosides of purines in poor yield.



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a	X = NH_2, Y = H	(229.3)	a	X = NH_2, Y = H	(281.3)
b	X = OH, Y = NH_2	(315.3)	b	X = OH, Y = NH_2	(297.3)
c	X = OH, Y = OH	(316.3)	c	X = OH, Y = OH	(298.3)
d	X = SH, Y = NH_2	(331.4)	d	X = SH, Y = NH_2	(313.4)
e	X = OH, Y = H	(300.3)	e	X = OH, Y = H	(282.3)
f	X = SH, Y = H	(316.4)	f	X = SH, Y = H	(298.4)

PROCEDURE

8,2'-Thioanhydroadenosine[b] (*2a*)[3]

8-Mercaptoadenosine[4] (*1a*) (24.0 g, 105 mmol) and diphenyl carbonate (20.5 g) are added to *N*,*N*-dimethylformamide (80 ml), and the solution is heated for 10 min at 150°. To the solution is added sodium hydrogen carbonate (300 mg), and the solution is heated until bubbling ceases. The solvent is removed *in vacuo*, and the residual gum is triturated with ether (300 ml). The resultant powder is suspended in ethanol (300 ml), and the suspension is

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[b] 8,2'-Anhydro-6-amino-9-β-D-arabinofuranosylpurine-8-thiol.

saturated with gaseous ammonia at 0° and then stirred for 5 hr at room temperature. The suspension is concentrated *in vacuo* to ≈200 ml, and the insoluble material is crystallized from a restricted volume of water (with activated charcoal) to give 10.38 g of the desired compound *2a*. An additional 4.0 g of crystals is obtained from the mother liquor. An analytical sample is obtained by recrystallization from water; m.p. 210° to 213° (melts at 140° to 150°, solidifies at 173°); $\lambda_{max}^{0.1\underline{M}\ HCl}$ 277 nm ($\varepsilon_{m\underline{M}}$ 20.10), $\lambda_{max}^{H_2O}$ 275.5 nm ($\varepsilon_{m\underline{M}}$ 20.30), 220.5 nm ($\varepsilon_{m\underline{M}}$ 19.30), $\lambda_{max}^{0.1\underline{M}\ NaOH}$ 276 nm ($\varepsilon_{m\underline{M}}$ 20.30), 220.5 nm ($\varepsilon_{m\underline{M}}$ 19.30).

8,2'-Thioanhydroguanosine[c] *(2b)*

By almost the same procedure as that used for preparing compound *2a*, 5.5 g of compound *2b* is obtained (from water) starting from 6.30 g (20 mmol) of 8-mercaptoguanosine[5] *(1b)*; m.p. >220° $\lambda_{max}^{0.1\underline{M}\ HCl}$ 267 nm ($\varepsilon_{m\underline{M}}$ 14.30), $\lambda_{max}^{H_2O}$ 265 nm ($\varepsilon_{m\underline{M}}$ 14.80), 280 nm (sh) ($\varepsilon_{m\underline{M}}$ 13.10), and $\lambda_{max}^{0.1\underline{M}\ NaOH}$ 279 nm ($\varepsilon_{m\underline{M}}$ 13.20).

8,2'-Thioanhydroxanthosine[d] *(2c)*

By almost the same procedure as that used for preparing compound *2a*, 780 mg of compound *2c* is obtained (from water) as fine needles, starting from 948 mg (3 mmol) of 8-mercaptoxanthosine[6] *(1c)*; m.p. (dec.) from 278°; $\lambda_{max}^{0.1\underline{M}\ HCl}$ 249 nm ($\varepsilon_{m\underline{M}}$ 12.30), 278 nm ($\varepsilon_{m\underline{M}}$ 13.00), $\lambda_{max}^{H_2O}$ 255 nm ($\varepsilon_{m\underline{M}}$ 13.40), 282 nm ($\varepsilon_{m\underline{M}}$ 12.60), $\lambda_{max}^{0.1\underline{M}\ NaOH}$

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[c] 8,2'-Anhydro-9-β-D-arabinofuranosyl-8-mercaptoguanine.

[d] 8,2'-Anhydro-9-β-D-arabinofuranosyl-8-mercaptoxanthine.

257.5 nm ($\varepsilon_{m\underline{M}}$ 14.00), 287 nm ($\varepsilon_{m\underline{M}}$ 13.30).

8,2'-Anhydro-(2-amino-9-β-D-ribofuranosylpurine-6-thiol)[e] *(2d)*

By almost the same procedure as that used for preparing compound *2a*, 4.70 g of *2d* is obtained (from water) starting from 6.29 g (19 mmol) of 2-amino-9-β-D-ribofuranosylpurine-6,8-dithiol[7] (*1d*); m.p. 220° to 228° (dec.); $\lambda_{max}^{0.1\underline{M}\ HCl}$ 235 nm ($\varepsilon_{m\underline{M}}$ 11.80), 261 nm ($\varepsilon_{m\underline{M}}$ 11.00), 355 nm ($\varepsilon_{m\underline{M}}$ 26.00), $\lambda_{max}^{H_2O}$ 235 nm ($\varepsilon_{m\underline{M}}$ 11.60), 261 nm ($\varepsilon_{m\underline{M}}$ 10.30), 355 nm ($\varepsilon_{m\underline{M}}$ 26.20), $\lambda_{max}^{0.1\underline{M}\ NaOH}$ 258 nm ($\varepsilon_{m\underline{M}}$ 16.30), 331 nm ($\varepsilon_{m\underline{M}}$ 22.30).

8,2'-Thioanhydroinosine[6] *(2e)*

By almost the same procedure as that used for preparing compound *2a*, 229 mg of compound *2e* is obtained (from a small volume of water) starting from 300 mg of 8-mercaptoinosine[4] (*1e*); m.p. dec. from 280°; $\lambda_{max}^{0.1\underline{M}\ HCl}$ 206.5 nm ($\varepsilon_{m\underline{M}}$ 15.30), 264 nm ($\varepsilon_{m\underline{M}}$ 16.40), $\lambda_{max}^{H_2O}$ 205 nm ($\varepsilon_{m\underline{M}}$ 15.10), 263.5 nm ($\varepsilon_{m\underline{M}}$ 16.30), 268 nm ($\varepsilon_{m\underline{M}}$ 16.90).

8,2'-Anhydro-9-β-D-ribofuranosylpurine-6-thiol[g] *(2f)*

By almost the same procedure as that used for preparing compound *2a*, 684 mg of crystalline *2f* is obtained (from 200 ml of water), starting from 1.79 g (5.7 mmol) of inosine-6,8-dithiol (*1f*); m.p. dec. from 251°; $\lambda_{max}^{0.1\underline{M}\ HCl}$ 251 nm ($\varepsilon_{m\underline{M}}$ 9.54), 336 nm ($\varepsilon_{m\underline{M}}$ 24.10), $\lambda_{max}^{H_2O}$ 250 nm ($\varepsilon_{m\underline{M}}$ 9.35), 336 nm ($\varepsilon_{m\underline{M}}$ 24.10), $\lambda_{max}^{0.1\underline{M}\ NaOH}$ 248.5 nm

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[e] 8,2'-Anhydro-(2-amino-9-β-D-arabinofuranosylpurine-6,8-dithiol).

[6] 8,2'-Anhydro-9-β-D-arabinofuranosyl-8-mercaptohypoxanthine .

[g] 8,2'-Anhydro-9-β-D-arabinofuranosylpurine-6,8-dithiol.

(ε_{mM} 14.70), 321 nm (ε_{mM} 24.80).

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